

IN THE SPECIFICATION:

Applicants, pursuant to 37 C.F.R. § 1.121, submit the following amendments to the Specification:

Kindly **substitute** the attached further amended SEQUENCE LISTING for that of applicants' last Response and Amendment of 21 April 2004 (no new matter has been added):

Additionally, please **substitute** the following paragraph for the corresponding paragraph on page 5, lines 9-26:

--Figure 1 shows a nucleotide sequence and amino acid of the insert in the extracellular domain of HER-2. The HER-2 ECD coding sequence from exon 1-9 (primers A and B) was amplified by PCR from a cDNA library from SKOV-3 cells. A product of ~1420 bp was found to be HER-2-specific by Southern blot analysis. This product was subcloned and the nucleotide sequence was determined. In panel A, ~~a the~~ nucleotide sequence (287 bp; SEQ ID NO:16) is shown for the 275 bp 274-bp insert (within the open-ended boxes outside the box) plus and for the immediately adjacent 5' and 3' sequences (framed by the open-ended boxes) enclosed in the box. The 275 bp insert sequence, using the numbering of Coussens et al. (Science 230:1132-1139, 1985), is located between nucleotide residues 1171 and 1172 and following amino acid residue 340 in p185HER-2 ~~using the numbering of Coussens et al. (Science 230:1132-1139, 1985).~~ SEQ ID NO:17 (276 bp) shows the 275 bp insert sequence plus the immediately 5' nucleotide ("G"). The consensus 5' and 3' splice sites at the arrows are shown in larger print. The inserted sequence is in-frame with 5' HER-2 exon sequence and is deduced to encode a 79 amino acid extension (SEQ ID NO:11) following Arg 340 (R<sup>340</sup>). The novel 79 ~~novel amino~~ acid sequence (SEQ ID NO:11) encoded by the insert is proline-rich (19%) and has a consensus asparagine linked glycosylation site, which is underlined. A stop codon was found at nucleotides 236-238 within the inserted sequence. In panel B, the predicted product of the alternative transcript is a truncated secreted protein which contains subdomains I and II identical to p185 and is missing the transmembrane domain and cytoplasmic domain. If fully glycosylated, the expected size is 65-70 kDa. This polypeptide product is referred to as p68HER-2. Thus, the product will be a truncated secreted protein which is missing the transmembrane domain and cytoplasmic domain found in p185HER-2.--

Additionally, please **substitute** the following paragraph for the corresponding paragraph on page 8, lines 9-15:

--Figure 8 shows the nucleotide (SEQ ID NO:18) and deduced amino acid sequence (SEQ ID NO:14) of HER-2 Intron 8. Human genomic DNA was subjected to PCR using primers that flank intron 8. PCR parameters were 30 cycles of 94 °C for 1 min, 62 °C for 1 min, 72 °C for 30 s, followed by 1 cycle of 72 °C for 7 min. A 410 bp product was gel purified and sequenced ~~sequence~~ in the forward and ~~an~~ reverse directions. The sequence shown is the most common sequence found within intron 8 from about 15 different individuals. Positions ~~The positions~~ of sequence variation resulting that would result in amino acid substitutions as disclosed herein are marked by Xs below the sequence.--